

U.S. Serial No. 08/887,505
Page 15 of 21

APPENDIX A

Pending Claims 1-33 and 42-43 (CLEAN VERSION)

1. (Amended) A synthetic oligonucleotide complementary to a portion of the 5' untranslated region of hepatitis C virus and having a nucleotide sequence selected from the group consisting of SEQ ID NOS:5, 6, 7, 8, 14, 15, 16, 23, 24, 26, 27, 28, 29, 31, 33, 36, 37, 47, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, and 133, as set forth in Table 1A, Table 1B, and Table 1F.
2. A synthetic oligonucleotide comprising a sequence complementary to at least two non-contiguous regions of an HCV messenger or genomic RNA.
3. An oligonucleotide according to claim 2, wherein the sequence is complementary to three non-contiguous regions.
4. A synthetic oligonucleotide according to claim 2, wherein one of the non-contiguous regions is the 5' untranslated region.
5. A synthetic oligonucleotide according to claim 3, wherein one of the non-contiguous regions is the 5' untranslated region.
6. An oligonucleotide according to claim 2 having about 18 to about 24 nucleotides.

U.S. Serial No. 08/887,505
Page 16 of 21

7. (Amended) An oligonucleotide according to claim 2, wherein one portion of the oligonucleotide has the sequence GGGGUCCUGGAG (SEQ ID NO:47) or has the sequence CAACACUACUCG (SEQ ID NO:80).
8. A synthetic oligonucleotide according to claims 1 or 2 which is modified.
9. An oligonucleotide according to claim 8, wherein the modification comprises at least one internucleotide linkage selected from the group consisting of alkylphosphonate, phosphorothioate, phosphorodithioate, alkylphosphonothioate, phosphoramidate, carbamate, carbonate, phosphate triester, acetamidate, carboxymethyl ester, and combinations thereof.
10. An oligonucleotide according to claim 9 comprising at least one phosphorothioate internucleotide linkage.
11. An oligonucleotide according to claim 9, wherein the internucleotide linkages in the oligonucleotide are phosphorothioate internucleotide linkages.
12. An oligonucleotide according to claim 8 which comprises at least one deoxyribonucleotide.
13. An oligonucleotide according to claim 8 which comprises at least one ribonucleotide.
14. An oligonucleotide according to claim 12 which additionally comprises at least one ribonucleotide.
15. An oligonucleotide according to claim 14, wherein an oligodeoxyribonucleotide region is interposed between two oligoribonucleotide regions, or the inverted configuration thereof.

U.S. Serial No. 08/887,505
Page 17 of 21

16. An oligonucleotide according to claim 13, wherein the ribonucleotide is a 2'-O-methyl ribonucleotide.
17. An oligonucleotide according to claim 14, wherein the ribonucleotide is a 2'-O-methyl ribonucleotide.
18. (Amended) An oligonucleotide according to claim 15, wherein the ribonucleotide is a 2'-O-methyl ribonucleotide.
19. An oligonucleotide according to claim 14 which comprises at least one 2'-O-methyl ribonucleotide at the 3'-end of the oligonucleotide.
20. An oligonucleotide according to claim 19 which further comprises at least one 2'-O-methyl ribonucleotide at the 5'-end of the oligonucleotide.
21. An oligonucleotide according to claim 14 having a nucleotide sequence, selected from the group consisting of SEQ ID NOS:119-130, as set forth in Table 1A.
22. (Amended) An oligonucleotide according to claim 2 comprising a sequence selected from the group consisting of SEQ ID NOS:38, 39, 40, 41, 42, 43, 44, 45, 46, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, and 67, as set forth in Table 2.
23. An oligonucleotide according to claim 2 comprising a sequence selected from the group consisting of SEQ ID NOS:134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146 and 147, as set forth in Table 1C.

U.S. Serial No. 08/887,505

Page 18 of 21

24. An oligonucleotide according to claim 3 comprising a sequence selected from the group consisting of SEQ ID NOS:148, 149, 150, 151, 152, 153, 154, 155, 156, 157, and 158, as set forth in Table 1D.
25. An oligonucleotide according to claim 8 which oligonucleotide is self stabilized by a loop.
26. (Amended) An oligonucleotide according to claim 24 having a sequence selected from the group consisting of SEQ ID NOS:131, 132, and 133, as set forth in Table 1B.
27. (Amended) An oligonucleotide according to claim 8, wherein the modification is selected from the group consisting of a nicked dumbbell, a closed dumbbell, 2', 3' and/or 5' caps, additions to the molecule at the internucleotide phosphate linkage, oxidation, oxidation/reduction, and oxidative/reductive amination, and combinations thereof.
28. An oligonucleotide according to claim 8, wherein at least one nucleoside is substituted by inosine or wherein at least one deoxycytosine is substituted by 5-methyl deoxycytosine.
29. (Amended) An oligonucleotide according to claim 28, wherein the oligonucleotide is selected from the group consisting of SEQ ID NOS:117 (HCV-242, HCV-243, HCV-244) and 118 (HCV-245), as set forth in Table 1A.
30. An oligonucleotide according to claim 8, wherein the oligonucleotide is modified by incorporating at least one additional triplex-forming strand.

U.S. Serial No. 08/887,505

Page 19 of 21

31. (Amended) An oligonucleotide according to claim 30 having a nucleotide sequence selected from the group consisting of SEQ ID NOS:159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171 and 172, as set forth in Table 1E.
32. A pharmaceutical composition comprising at least one oligonucleotide according to claim 1 and a pharmacologically acceptable carrier.
33. A pharmaceutical composition comprising at least one oligonucleotide according to claim 2 and a pharmaceutically acceptable carrier.
42. (New) A pharmaceutical composition comprising at least two different oligonucleotides according to claim 1 in a pharmacologically acceptable carrier.
43. (New) A pharmaceutical composition comprising at least two different oligonucleotides according to claim 2 in a pharmacologically acceptable carrier.

U.S. Serial No. 08/887,505
Page 20 of 21

APPENDIX B

Amended Claims 1, 7, 18, 22, 26, 27, 29, 31 and New Claims 42-43 (MARKED UP VERSION)

1. (Amended) A synthetic oligonucleotide complementary to a portion of the 5' untranslated region of hepatitis C virus and having a nucleotide sequence selected from the group consisting of SEQ ID NOS:[2,]5, 6, 7, 8, 14, 15, 16, 23, 24, 26, 27, 28, 29, 31, 33, 36, 37, 47, 68, 69, 70, 71, 72, 73, 74, 75, 76, [and] 77, [as set forth in Table 1F and selected from the group consisting of SEQ ID NOS.]78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, [108. 109] 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, and 133, as set forth in Table 1A [and], Table 1B, and Table 1F.
7. (Amended) An oligonucleotide according to claim 2, wherein one portion of the oligonucleotide has the sequence GGGGUCCUGGAG (SEQ ID NO:47) or has the sequence CAACACUACUCG (SEQ ID NO:80).
18. (Amended) An oligonucleotide according to [laim] claim 15, wherein the ribonucleotide is a 2'-O-methyl ribonucleotide.
22. (Amended) An oligonucleotide according to claim 2 comprising a sequence selected from the group consisting of SEQ ID NOS:38, 39, 40, 41, 42, 43, 44, 45, 46, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, and 67, as set forth in Table 2.

U.S. Serial No. 08/887,505

Page 21 of 21

26. (Amended) An oligonucleotide according to claim 24 having a sequence selected from the group consisting of SEQ ID NOS:131, 132, and 133, as set forth in Table 1B.
27. (Amended) An oligonucleotide according to claim 8, wherein the modification is selected from the group consisting of a nicked dumbbell, a closed dumbbell, 2', 3' and/or 5' caps, additions to the molecule at the internucleotide phosphate linkage, oxidation, oxidation/reduction, and oxidative/reductive amination, [including combination] and combinations thereof.
29. (Amended) An oligonucleotide according to claim 28, wherein the oligonucleotide is selected from the group consisting of SEQ ID NOS:117 [(HCV -242, HCV 243, HCV -244)] (HCV-242, HCV-243, HCV-244) and 118 [(HCV -245)] (HCV-245), as set forth in Table 1A.
31. (Amended) An oligonucleotide according to claim 30 having a nucleotide sequence selected from the group consisting of SEQ ID NOS:159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171 and 172, as set forth in Table 1E.
- 42. (New) A pharmaceutical composition comprising at least two different oligonucleotides according to claim 1 in a pharmacologically acceptable carrier.
43. (New) A pharmaceutical composition comprising at least two different oligonucleotides according to claim 2 in a pharmacologically acceptable carrier.--

WASHINGTON 154194v2